

Flag-peptide GAD65 Not I IA2 Not I PPINS poly-his
 DYKDDDDK-----~~Sgf I~~-----KKRPRKKK-----KKRPRKKK-----CNGSHHHHHH

FIG. 1a

Flag-peptide GAD65 Sgf I IA2 Sgf I PPINS poly-his
 DYKDDDDK-----~~Not I~~-----KKRPRKKK-----KKRPRKKK-----CNGSHHHHHH

FIG. 1b

~~1A2 Underlined aa 771-979 Accession No. L18983~~

MRRPRRPGGLGGGLRLLCLLLSSRPGGCSA VSAHGCLFDRRLCSHLEVCIQDGLFGQCQVGVQARPLLQVTSPVLQRL
QGVLRQLMSQGLSWHDDL TQYVISQEMERIPRLRPEPRDRSGLAPKRPAGAGELLQDIPTGSAPAAQHRLPQPPVGKGG
AGASSLSPLQAELLPPLLEHLLPPQPPHPSLSYEPALLQPYLFHQFGRDGSRVSEGSPGMVSVGPLPKAEAPALFSRTASKGI
FGDHPGHSYGDLPGPSAQLFQDSGLLYLAQELPAPSRARVPRLPEQGSSRAEDSPGEYEKEGLGDRGEKPASPAVQPDAAAL
QRLAAVLAGYGVELRQLTPEQLSTLLTLQLLPKAGRNPGGVNVGADIKKTMGPVEGRDTAELPARTSPMPGHPTASPT
SSEVQQVPSVSSEPPKAAARPPVTPVLEKKSPLGQSQT VAGQPSARPAAEYGYIVTDQKPLSLAAAGVKKLEILAEHVHMSS
GSFINISVVGPA LTFRIRHNEQNLSLADVTQAGLVKSELEAQTGLQILQTGVGQREEA AVLPQTAHSTSPMRSVLLTLVVALA
GVAGLLVALAVALCVRQHARQQDKERLAALGPEGAGDITFEYQDLCRQHMA TKSLFNR AEGPEPSRVSSVSSQFSDA AQ
ASSSHSTPSWCEEPAQANMDISTGHMILAYMEDHLNRDRRLAKEWQALCA YQAEPN TCATAQEGEKNKNRHPDFLPYDH
ARIKLVESPSRSDYINASPIEHDPMPAYIATQGPLSHTIADFWQMVWESGCTIVVMLTPLVEDGVKQCDRYWPDEGASLY
HVYEVN LVSEHIWCEDFLVRSFYLNKVNOTOETRTLTOHFLSWPAEGTPASTRPLLD FRRKVNKCYGRSCPIIVHCSDGAGR
TGTYILDMVLNRMAKGVKEIDIAATLEHVDRDQRPGLVRSKDQFEFALTAVAEVNAILKALPQ

FIG. 2a

~~GAD65 Underlined aa102-585 Accession No. M74826~~

MASPGSFWFSGEDSGDSENPGTARAWCQVAQKFTGGIGNKLCALLYGDAEKP AESGGSQPPRAAARKAACACDQKPCS
CSKVDVNYAFLHATDLLPACDGERPTLAFLQDVMNILLQYVVKSFDRSTKVDFHYPNELLOEYNWELADQPQNLEEILMHC
QTTLKYAIKTGHPRYFNQLSTGLDMVGLAADWL TSTANTNMFTYEIAPVFLLEYVTLKKMREIIGWPGSGDGIFSPGGAIS
NMYAMMIARFKMFPEVKEKGMAALPRLIAFTSEHSHFSLKKGAAALGIGTDSVILIKCDERGKMIPSDLERRILEAKOKGFVPP
LVSATAGTTVYGAFDPLLA VADICKKYKIWMHVDAAWGGGLMSRKHKWKLSGVERANSVTWNP HKMMGVPLQCSALLY
REEGLMONCNQM HASYLFQODKHYDLSYDTGDKALOCGRHVDVFKLWLMWRAKGTTGFEAHVDKCLEAEYL YNIIKNR
EGYEMVFDGKPOHTNVCFWYIPPSLRTLEDNEERM SRLSKVAPVIKARMMEYGTMTVSYOPLGDKVNFFRMVISNPAATHQ
DIDFLIEEIERLGODL

FIG. 2b

~~Translation Human preproinsulin.~~

~~EMBL accession nr. v00565~~

MALWMRLPLALLALWGPDPAAAFVNQHL CGSHLVEALYLVCGERGFFYT
PKTRREAEDLQVGQVELGGPGAGSLQPLALEGSLQKRGIVEQCCTSI CSLYQ
LENYCN

FIG. 2c

5N 09/015397

~~Human GAD65 nucleotide sequence~~~~M74826 Length: 2457 September 1, 1995 12:22 Type: N Check: 8038 ..~~

1 ACCCGCCCTC GCCGCTCGGC CCCGCGCGTC CCCGCGCGTG CCTCTCTCC
51 GCCACACGGC ACGCACGCGC GCGCAGGGCC AAGCCGAGGC AGCCGCCCGC
101 AGCTCGCACT CGCTGGCGAC CTGCTCCAGT CTCCAAAGCC GATGGCATCT
151 CCGGGCTCTG GCTTTTGGTC TTTCGGGTCG GAAGATGGCT CTGGGGATTC
201 CGAGAATCCC GGCACAGCGC GAGCCTGGTG CCAAGTGGCT CAGAAGTTCA
251 CGGGCGGCAT CGGAAACAAA CTGTGCGCCC TGCTCTACGG AGACGCCGAG
301 AAGCCGGCGG AGAGCGGCGG GAGCCAACCC CCGCGGGCCG CCGCCCGGAA
351 GGCCGCCTGC GCCTGCGACC AGAAGCCCTG CAGCTGCTCC AAAGTGGATG
401 TCAACTACGC GTTCTCCAT GCAACAGACC TGCTGCCGGC GTGTGATGGA

451 GAAAGGCCCA CTTTGGCGTT TCTGCAAGAT GTTATGAACA TTTTACTTCA
501 GTATGTGGTG AAAAGTTTCG ATAGATCAAC CAAAGTGATT GATTTCATT
551 ATCCTAATGA GCTTCTCCAA GAATATAATT GGAATTGGC AGACCAACCA
601 CAAAATTTGG AGGAAATTTT GATGCATTGC CAAACAACCTC TAAAATATGC
651 AATTAAACAA GGGCATCCTA GATACTTCAA TCAACTTTCT ACTGGTTTGG
701 ATATGGTTGG ATTAGCAGCA GACTGGCTGA CATCAACAGC AAATACTAAC
751 ATGTTACCT ATGAAATTGC TCCAGTATTT GTGCTTTTGG AATATGTCAC
801 ACTAAAGAAA ATGAGAGAAA TCATTGGCTG GCCAGGGGGC TCTGGCGATG
851 GGATATTTTC TCCCGGTGGC GCCATATCTA ACATGTATGC CATGATGATC
901 GCACGCTTTA AGATGTTCCC AGAAGTCAAG GAGAAAGGAA TGGCTGCTCT
951 TCCAGGCTC ATTGCCTTCA CGTCTGAACA TAGTCATTTT TCTCTCAAGA
1001 AGGGAGCTGC AGCCTTAGGG ATTGGAACAG ACAGCGTGAT TCTGATTAAA
1051 TGTGATGAGA GAGGGAAAAT GATTCCATCT GATCTTGAAA GAAGGATTCT
1101 TGAAGCCAAA CAGAAAGGGT TTGTTCTTTT CCTCGTGAGT GCCACAGCTG
1151 GAACCACCGT GTACGGAGCA TTTGACCCCC TCTTAGCTGT CGCTGACATT
1201 TGCAAAAAGT ATAAGATCTG GATGCATGTG GATGCAGCTT GGGGTGGGGG
1251 ATTACTGATG TCCCGAAAAC ACAAGTGGA ACTGAGTGGC GTGGAGAGGG

FIG. 3a

~~Human IA-2 nucleotide sequence~~~~L18983 Length: 3613 November 20, 1997 16:45 Type: N Check: 6409 ..~~

1 CAGCCCCTCT GGCAGGCTCC CGCCAGCGTC GCTGCGGCTC CGGCCCGGGA
51 GCGAGCGCCC GGAGCTCGGA AAGATGCGGC GCCCGCGGCG GCCTGGGGGT
101 CTCGGGGGAT CCGGGGGTCT CCGGCTGCTC CTCTGCCTCC TGCTGCTGAG
151 CAGCCGCCCC GGGGGCTGCA GCGCCGTTAG TGCCACGGC TGTCTATTTG
201 ACCGCAGGCT CTGCTCTCAC CTGGAAGTCT GTATTCAGGA TGGCTTGTTT
251 GGGCAGTGCC AGGTGGGAGT GGGGCAGGCC CGGCCCTTT TGCAAGTCAC
301 CTCCCCAGTT CTCAACGCT TACAAGGTGT GCTCCGACAA CTCATGTCCC
351 AAGGATTGTC CTGGCACGAT GACCTCACCC AGTATGTGAT CTCTCAGGAG
401 ATGGAGCGCA TCCCCAGGCT TCGCCCCCA GAGCCCCGTC CAAGGGACAG
451 GTCTGGCTTG GCACCAAGA GACCTGGTCC TGCTGGAGAG CTGCTTTTAC
501 AGGACATCCC CACTGGCTCC GCCCCTGCTG CCCAGCATCG GCTTCCACAA
551 CCACCAGTGG GCAAAGGTGG AGCTGGGGCC AGCTCCTCTC TGTCCCCTCT
601 GCAGGCTGAG CTGCTCCCGC CTCTCTTGGA GCACCTGCTG CTGCCCCCAC
651 AGCCTCCCCA CCCTTCACTG AGTTACGAAC CTGCCTTGCT GCAGCCCTAC
701 CTGTTCCACC AGTTTGGCTC CCGTGATGGC TCCAGGGTCT CAGAGGGCTC
751 CCCAGGGATG GTCAGTGTG GCCCCCTGCC CAAGGCTGAA GCCCCTGCCC
801 TCTTCAGCAG AACTGCCTCC AAGGGCATAT TTGGGGACCA CCCTGGCCAC
851 TCCTACGGGG ACCTTCCAGG GCCTTACCT GCCCAGCTTT TTCAAGACTC
901 TGGGCTGCTC TATCTGGCCC AGGAGTTGCC AGCACCCAGC AGGGCCAGGG
951 TGCCAAGGCT GCCAGAGCAA GGGAGCAGCA GCCGGGCAGA GGAATCCCCA
1001 GAGGGCTATG AGAAGGAAGG ACTAGGGGAT CGTGGAGAGA AGCCTGCTTC
1051 CCCAGCTGTG CAGCCAGATG CGGCTCTGCA GAGGCTGGCC GCTGTGCTGG
1101 CGGGCTATGG GGTAGAGCTG CGTCAGCTGA CCCCTGAGCA GCTCTCCACA
1151 CTCCTGACCC TGCTGCAGCT ACTGCCAAG GGTGCAGGAA GAAATCCGGG
1201 AGGGGTTGTA AATGTTGGAG CTGATATCAA GAAAACAATG GAGGGGCCGG
1251 TGGAGGGCAG AGACACAGCA GAGCTTCCAG CCCGCACATC CCCCATGCCT

FIG. 3c

~~PREPROINSULIN~~~~Exon sequences, i.e. sequences to be used in the patent are underlined and represent exon sequences.~~~~V00565 Length: 4992 December 18, 1997 17:50 Type: N Check: 9721 ..~~

1 CTCGAGGGGC CTAGACATTG CCCTCCAGAG AGAGCACCCA ACACCCTCCA
51 GGCTTGACCG GCCAGGGTGT CCCCTTCCTA CTTGGAGAG AGCAGCCCCA
101 GGGCATCCTG CAGGGGGTGC TGGGACACCA GCTGGCCTTC AAGGTCTCTG
151 CCTCCCTCCA GCCACCCAC TACACGCTGC TGGGATCCTG GATCTCAGCT
201 CCCTGGCCGA CAACACTGGC AAACCTCTAC TCATCCACGA AGGCCCTCCT
251 GGGCATGGTG GTCCTTCCCA GCCTGGCAGT CTGTTCTCTA CACACCTTGT
301 TAGTGCCAG CCCCTGAGGT TGCAGCTGGG GGTGTCTCTG AAGGGCTGTG
351 AGCCCCCAGG AAGCCCTGGG GAAGTGCCTG CTTGCCTCC CCCCGGCCCT
401 GCCAGCGCCT GGCTCTGCCC TCCTACCTGG GCTCCCCCA TCCAGCCTCC
451 CTCCCTACAC ACTCCTCTCA AGGAGGCACC CATGTCCTCT CCAGCTGCCG
501 GGCCTCAGAG CACTGTGGCG TCCTGGGGCA GCCACCGCAT GTCCTGCTGT
551 GGCATGGCTC AGGGTGAAA GGGCGGAAGG GAGGGGTCCT GCAGATAGCT
601 GGTGCCCCT ACCAAACCCG CTCGGGGCAG GAGAGCCAAA GGCTGGGTGT
651 GTGCAGAGCG GCCCCGAGAG GTTCCGAGGC TGAGGCCAGG GTGGGACATA
701 GGGATGCGAG GGGCCGGGGC ACAGGATACT CCAACCTGCC TGCCCCCATG
751 GTCTCATCCT CCTGCTTCTG GGACCTCCTG ATCCTGCCCC TGGTGCTAAG
801 AGGCAGGTAA GGGGCTGCAG GCAGCAGGGC TCGGAGCCCA TGCCCCCTCA
851 CCATGGGTCA GGCTGGACCT CCAGGTGCCT GTTCTGGGGA GCTGGGAGGG
901 CCGGAGGGGT GTACCCAGG GGCTCAGCCC AGATGACACT ATGGGGGTGA
951 TGGTGTCATG GGACCTGGCC AGGAGAGGGG AGATGGGCTC CCAGAAGAGG
1001 AGTGGGGGCT GAGAGGGTGC CTGGGGGGCC AGGACGGAGC TGGGCCAGTG
1051 CACAGCTTCC CACACCTGCC CACCCCAGA GTCCTGCCGC CACCCCAGA
1101 TCACACGGA GATGAGGTCC GAGTGGCCTG CTGAGGACTT GCTGCTTGTC
1151 CCCAGGTCCC CAGGTCATGC CCTCCTTCTG CCACCCTGGG GAGCTGAGGG
1201 CCTCAGCTGG GGCTGCTGTC CTAAGGCAGG GTGGGAACTA GGCAGCCAGC
1251 AGGGAGGGGA CCCCTCCCTC ACTCCCACTC TCCCACCCC ACCACCTTGG
1301 CCCATCCATG GCGGCATCTT GGGCCATCCG GGAAGGGGA CAGGGGTCTT
1351 GGGGACAGGG GTCCGGGGAC AGGGTCCTGG GGACAGGGGT GTGGGGACAG

FIG. 3f